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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,299	09/22/2006	Kameron W. Maxwell	MITOS.004NP	4357

20995 7590 10/29/2008

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EXAMINER	
RAE, CHARLESWORTH E	
ART UNIT	**PAPER NUMBER**
1611	

NOTIFICATION DATE	DELIVERY MODE
10/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/554,299	MAXWELL, KAMERON W.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 32-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 32-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 07/14/08, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Status of the Claims

Claims 1-15, and 32-47 are currently pending in this application.

Claims 32-47 are new.

Amendment of the Specification

Receipt of applicant's amendment to the specification is acknowledged and entered of record. Applicant's statement that said amendment was made to correct a typographical error is duly noted (see applicant's Response, received 07/14/08, page 15, first para.).

Response to applicant's arguments/remarks

Rejection under 101

This rejection is withdrawn in view of the claim amendment canceling claims 16-23.

Rejection under 112, 2nd paragraph

This rejection is withdrawn in view of the claim amendment canceling claims 16-23.

Nonstatuotry obviousness-type double patenting (ODP) rejection

These rejections are withdrawn (see applicant's Response, received 07/14/08, pages 15-16).

Scope of enablement rejection under 112, 1st paragraph

Applicant contends that this rejection should be withdrawn (see applicant's Response, page 16-17).

In response, this rejection is maintained as applicant's arguments are not found to be sufficiently persuasive to overcome the rejection made of record in the Office action, mailed 03/21/08, at pages 5-9, and for the additional reason set forth below.

a) Contrary to applicant's arguments, it is the examiner's position that the term "identify a human patient that is susceptible" given its broadest reasonable possible interpretation in light of the instant specification reasonably encompasses human patients without ischemia, including normal healthy humans, because the effect to be achieved by practicing the instant invention i.e. "prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia" necessarily requires the absence of an ischemic event prior to the step of administering a nitroxide to a human patient. Besides, the step of "identify a human patient that is susceptible" reasonably encompass various invasive and non-invasive medical procedures which may vary significantly in predictably identifying humans with ischemia, including silent ischemia (see instant specification, page 3, para. 0017).

b) The term “ischemia” as defined in general terms in the instant application and does not comport with applicant's asserted limited interpretation of said term (see specification, page 2, para. 0009, lines 3-5).

c) Although the instant specification provides support for a method of reducing the harmful effects of ischemia in human patient who is susceptible to ischemia by administering a sufficient amount of a nitroxide to said patient prior to the onset ischemia, it does not reasonably provide enablement for preventing a harmful effect of ischemia in all tissues/organs in a human patient prior to the onset of ischemia as further evidenced by the teaching of Stern S. (Stern S. Angina Pectoris without chest pain: clinical implications of silent ischemia. Circulation. 2002;106:1906-1908).

d) Stern discloses that in clinical studies as many as 90% of ischemic episodes were found to be silent (page 1906, col. 1, first full para.). Also, Stern teaches that ambulatory monitoring does not appear to be useful for screening or for primary detection of ischemic heart disease (IHD) (page 1907, col. 1, lines 3-6).

Thus, there is reasonably doubt that an artisan skilled in the art would have been able to practice the instant claimed invention commensurate with the scope of the claims without conducting undue experimentation

Rejection under 102

This rejection is withdrawn as applicant's arguments are found to be persuasive (see applicant’s Response, pages 17-18).

REJECTIONS

Claim rejections – 35 USC 112 – Second Paragraph

The following is a quotation of the second paragraph of 35 USC 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 32 recites extraneous hand written subject matter which renders the claimed subject matter indefinite because it is unclear what the term "R2" specifically means in view of the extraneous subject matter included therein (see page 5 of claim amendment, fourth line from the bottom of page).

It is noted that applicant is requested to submit a clean copy of the instant claims.

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15, and 32-47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-17, and 19-25 of copending U.S. Patent Application No. 10/675,225, in view of Stern as discussed above.

In particular, reference claim 16 recites “[a] method of treating a patient, comprising topically applying a sufficient amount of a nitroxide radioprotector to prevent or treat harmful side effects caused by radiotherapy, wherein the nitroxide

radioprotector is in solution in a solvent, and the solution is in the form of a low-residue gel or a low-residue thickened liquid." Reference claim 17, for example, recites the identical compound as recited in instant claim 2. Unlike the instant claims, the reference claims do not recite the step of identifying a human patient that is susceptible to ischemia. It is the examiner's position the instant claim term "human patient susceptible to ischemia" reasonably encompasses all human patients, including the reference patient population. Further, the reference step of topically applying a sufficient amount of a nitroxide radioprotector (e.g. 4-hydroxy-2,2-6,6-tetramethylpiperidien-1-oxyl; see reference claims 16-17) to prevent or treat harmful side effects caused by radiotherapy is capable of performing the intended function i.e. preventing a harmful effect of ischemia in a human patient prior to the onset of ischemia. The discussion of Stern in connection with the rejection under 103(a) is incorporated by reference. Despite the difference between the reference claims and the instant claims, it would have been obvious to a person of skill in the art at the time the invention was made to first identify a high-risk male human patient with ischemic heart disease (IHD) prior to scheduling said high-risk male human patient to a medical procedure (e.g. exercise testing) as taught by Stern, followed by the reference method of treatment comprising administering 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) in order to control ischemia. One would have been motivated to first identify a high-risk male human patient with ischemic heart disease (IHD) and schedule said high-risk male human patient to a medical procedure (e.g. exercise testing) in order to accurately diagnose IHD because Stern suggest that medical procedures (e.g. exercise

testing) can identify high-risk men, even asymptomatic men, with IHD (e.g. myocardial infarction). Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Claim Rejections – 35 USC 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 and 32-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for methods of reducing the harmful effects of ischemia comprising administering Tempol, does not reasonably provide enablement for preventing a harmful effect of ischemia in a human patient prior to the onset of ischemia by administering all nitroxide compounds to said patient. This is a scope of enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without

undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if its is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth in *In re Wands,* 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman* 230 USPQ 546 (BdApls 1986) at 547 the court cited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, state and predictability of the art, and relative skill of those in the art.

The invention in general relates to a method of treatment comprising identifying a human patient that is susceptible to ischemia and administering a sufficient amount of a nitroxide to prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia.

The state and predictability of the art

Herfindal et la. teach that ischemia refers to a lack of oxygen secondary to reduced perfusion (Herfindal et al. (eds.). Clinical Pharmacy and Therapeutics. 1992, pages 677-707, and 709; see page 677, first para). Herfindal et al. also teach that myocardial ischemia is caused by an imbalance between oxygen supply and demand usually as a result of atherosclerosis in the large epicardial coronary arteries; it may also occur as a consequence of either focal or generalized vasospasm of the major coronary arteries (page 677, first para.). Thus, any and all tissues/organs would reasonably be susceptible to “ischemia” wherein the perfusion of blood to said tissues/organs is reduced. It necessarily follows, that ischemia to said tissues/organs would necessarily result in a lack of oxygen secondary to reduced blood perfusion.

Stern (Stern S. Angina Pectoris without chest pain: clinical implications of silent ischemia. Circulation. 2002;106:1906-1908) teach that exercise testing can identify high- risk men, even if asymptomatic, who could benefit from risk reduction and preventive measures (page 1907, especially col. 1, first full para.). However, Stern also teach that it is unfortunate that increased awareness and improved diagnosis if silent IHD over the years has not thus far decreased the incidence of unrecognized MI (page 1907, col. 1, last four lines).

The relative skill of those in the art

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. It is noted that the chemical and medical arts are generally unpredictable, requiring each embodiment to be individually assessed for chemical, pharmacologic, pharmaceutical, and clinical efficacy. The more unpredictable an area, the more specific enablement is necessary in order to satisfy the statue. (see *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970)). Despite the level of skill of those in the art, the incidence of unrecognized MI has not apparently changed over the past the years (see above discussion regarding Stern). Thus, it is doubtful that in the absence of evidence to show a correlation between the contemplated effect to be achieved (.i.e. preventing ischemia or harmful effects of ischemia) in practicing the instant method and a common critical chemical feature of members of the genus of nitroxide compounds that an artisan would be able to reasonably practice the invention commensurate with the scope of claims with respect to all nitroxide compounds without conducting extensive experimentation.

The breadth of the claims

The instant claims are relatively broad in scope. For example, claim 1 recites “[a] method of treatment, comprising administering a sufficient amount of a nitroxide” reasonably encompasses a multiplicity of different routes of drug administration, including intravenous, intracoronary, topical drug administration, which could significantly affect the onset of action of the drug depending on the specific route of administration employed. Also, the adverse effects associated with intracornoary administration of a drug would vary significantly from the adverse effects observed with topical administration of the same dose of the drug. Further, the term “a nitroxide,”given its broadest reasonable possible interpretation encompasses any and all compounds with a nitroxide structural component therein. Claim 1 also recite the term “a sufficient amount of a nitroxide to prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia;" however, it is unclear what amount of a nitroxide, if any, can prevent any and all harmful effects of ischemia in the human patient (see instant specification, page 8). The term "prophylactic or therapeutic amount of nitroxide to ameliorate a harmful effect of ischemia" recited in claim 9, and the term “prevent a harmful effect of ischemia through administration to a mammalian patient prior to the onset of ischemia” as recited in claim 16 are also very broad and are not found to be supported by the instant disclosure. Besides, the harmful effects of ischemia in a human patient would vary significantly depending on the specific location of the ischemic event. For instance, the harmful effects of brain ischemia (i.e. strokes) vary significantly from the harmful effects of ischemia involving the heart (e.g. myocardial ischemia).

The amount of direction or guidance provided and the presence or absence of working

Examples

Applicant discloses that patients who were given Tempol prior to and after treatment for aneurysmal subarachnoid hemorrhaging have fewer and smaller sized infracts than patients who only receive placebo (page 12, para. 0058, Example 1). Applicant discloses that generally nitroxides can prevent or ameliorate any effect of ischemia in a patient (page 5, para. 0025). Applicant asserts methods to prevent or ameliorate any effect of cardiac ischemia, myocardial ischemia, ... (specification, para. 0022). Example 1 describes a clinical study protocol to determine the effect of Tempol on the prevention of cerebral ischemia, which appears to be an invitation to conduct further experimentation (specification, page 12-13). Based on the instant disclosure, the applicant at best has provided specific direction or guidance only for a general method of treating a patient suspected of ischemia comprising administering a sufficient amount of a nitroxide because applicant has only shown the effect o Tempol in achieving the claimed end treatment result; however, showing enablement for single species does not render the entire nitroxide compound genus enabled. To the extent that the end treatment results would vary significantly depending on the specific site of ischemia, it is doubtful that an artisan skilled in the art would able to reasonably practice the instant invention commensurate with the scope of the claims without resorting to undue experimentation in the absence of evidence to show a correlation between the structure of nitroxide compounds and the end treatment result that is intended to be achieved in practicing the instant invention.

The quantity of experimentation necessary

In view of the uncertainty and unpredictability of in the medical art, coupled with the wide breadth of the claims, it is reasonable to surmise that the level of uncertainty in the art would require one skilled in the art to conduct more than routine experimentation in order to practice the claimed invention commensurate with the scope of the claims.

For the reasons stated above, claims 1-15, and 32-47 are rejected under 35 USC 112, first paragraph, for lack of scope enablement because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with the claims.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

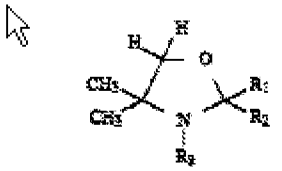
the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15, and 32-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mitchell et al. (US Patent 5,462,946; already made of record), in view of Stern S. (Stern S. Angina Pectoris without chest pain: clinical implications of silent ischemia. Circulation. 2002;106:1906-1908) and, as evidenced by Herfindal et al. (Herfindal et al. (eds.). Clinical Pharmacy and Therapeutics. 1992, pages 677-707, and 709; see page 677, first para; already made of record).

Claim 1 recites "[a] method of treatment, comprising: identifying a human patient that is susceptible to ischemia; and administering a sufficient amount of a nitroxide to prevent a harmful effect of ischemia in the human patient prior to the onset of ischemia." Claim 9 recites "[a] method of treatment comprising: identifying a patient scheduled to undergo a medical procedure involving a significant risk of ischemia; administering to the patient, prior to the medical procedure, a prophylactic amount of nitroxide; performing the medical procedure; and administering to the patient, a prophylactic or therapeutic amount of nitroxide to ameliorate a harmful effect of ischemia." Claim 34 recites 34 [a] method of treatment, comprising: identifying a human patient that is

susceptible to ischemia; and administering a sufficient amount of a nitroxide to reduce a harmful effect of ischemia in the human patient prior to the onset of ischemia, wherein the nitroxide is selected from the group consisting of …" Claim 42 recites [a] method of treatment comprising: identifying a patient scheduled to undergo a medical procedure involving a significant risk of ischemia; administering to the patient, prior to the medical procedure, a sufficient amount of a nitroxide to reduce a harmful effect of ischemia in the human patient; performing the medical procedure; and administering to the patient after the performing step, an amount of nitroxide to reduce a harmful effect of ischemia; wherein the nitroxide is selected from the group consisting of …"

Mitchell et al. (US Patent 5,462,946) teach intravenous administration of compounds having the below formula, including 2,2,6,6-tetramethylpiperidine-1-oxyl (also known as TEMPO) and the elected compound, 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (also know as TEMPOL), for use as a protectant against oxidative stress in treating various conditions associated with oxidative stress such as reperfusion injury,strokes, myocardial infraction, wherein said compounds are administered intravenously in an amount of about 0.01 to about 300 mg/kg/day (see abstract; col. 2, 62 to col. 3, line 10; and col. 4, line 43 to col. 5, line 58):



wherein R_1 is $—CH_3$; R_2 is $—C_2H_5$, $—C_3H_7$, $—C_4H_9$, $—C_5H_{11}$, $—C_6H_{13}$, $—CH_2—CH(CH_3)_2$, $—CHCH_3C_2H_5$, or $—(CH_2)_7—CH_3$, or wherein R_1 and R_2 together form spirocyclopentane, spirocyclohexane, spirocycloheptane, spirocyclooctane, 5-cholestane, or norbornane, R_3 is —O, or —OH, or a physiologically acceptable salt thereof, and a pharmaceutically acceptable carrier, as antioxidants capable of protecting cells, tissues, organs, and whole organisms against the deleterious effects of harmful oxygen-derived species generated during oxidative stress.

However, Mitchell et al. is silent regarding the instant step of identifying a human patient that is susceptible to ischemia.

Stern is added to show the risk associated with ischemia. Stern et al. that exercise testing can identify high- risk men, even if asymptomatic, who could benefit from risk reduction and preventive measures (page 1907, especially col. 1, first full para.). Stern teaches that myocardial defects detected on stress thallium testing or ventricular dysfunction seen on stress examinations are accepted as evidence for transient ischemia, despite the lack of both accompanying ECG alterations and chest pain (page 1907, col. 1, second full para.). Stern teaches that because myocardial infarction (MI) may be silent, awareness is called for when sudden unexplained cardiac symptoms appear (page 1907, col. 2, conclusion section).

Herfindal et al. is added as an evidentiary reference only to show that ischemia means a lack of oxygen secondary to reduced perfusion. Herfindal et al. teach that ischemia refers to a lack of oxygen secondary to reduced perfusion (Herfindal et al. (eds.). Clinical Pharmacy and Therapeutics. 1992, pages 677-707, and 709; see page 677, first para). Herfindal et al. also teach that myocardial ischemia is caused by an imbalance between oxygen supply and demand usually as a result of atherosclerosis in the large epicardial coronary arteries; it may also occur as a consequence of either focal or generalized vasospasm of the major coronary arteries (page 677, first para.).

It would have been obvious to a person of skill in the art at the time the invention was made to identify a person at risk of ischemia as taught by Stern prior to treating a patient with reperfusion injury (e.g. MI) by administering 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) as taught by Mitchell et al. One would have been motivated to identify a patient susceptible to ischemia and then administer 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl because Stern suggests that testing can identify high risk men, even if asymptomatic, who could benefit from risk reduction and preventive measures. Besides, it is the examiner's position that it is routine in the art to first diagnose (= identify) a patient with ischemia (e.g. myocardial infarction) prior to administering treatment for said myocardial infarction i.e. diagnostic tests by definition are performed routinely in the medical art to diagnose patients with specific conditions (= functional equivalent of identifying a patient with a specific condition e.g. ischemia). One would have expected to successfully identify a patient susceptible for ischemia, then treating said patient by administering 4-

hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) because Mitchell et al. teach 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL) for use as a protectant against oxidative stress in treating various conditions associated with oxidative stress such as reperfusion injury (e.g. MI) and strokes, wherein said compounds are administered intravenously in an amount of about 0.01 to about 300 mg/kg/day (see abstract; col. 2, 62 to col. 3, line 10; and col. 4, line 43 to col. 5, line 58) and myocardial infarction is an oxidative stress as evidenced by the teaching of Herfindal et al. and the dose taught by the prior art overlaps with the dose of Tempol disclosed in the instant application. Further, one would have also expected to successfully treat any patient that is identified as being susceptible to ischemia, including patients wherein the susceptibility arises from a medical procedure associated with a significant ischemic risk (e.g. treatment of hemorrhage, aneurysm, and endovascular procedure), as Mitchell et al. provides a general teaching of ischemia and therefore one of skill in the art would reasonably have expected to achieve similar end treatment results (i.e. reducing a harmful effect of ischemia) by administering 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) to any patient identified as being susceptible to ischemia from others etiologic causes (e.g. ischemia associated with treatment of hemorrhage/ aneurysm/ and endovascular procedure).

It is noted that it is the examiner's position that it would have been within the skill and knowledge of an artisan skilled in the art to identify a patient susceptible of ischemia associated with medical procedures, including medical procedures for treating

hemorrhage, aneurysm, as well as ischemia associated with endovascular procedures, without resorting to undue experimentation in the absence of evidence to show the contrary.

It is also noted that the term 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) as taught by Mitchell et al. reads on the nitroxide component recited in claims 1, 2, 10, 32, 33, 34, 35, 42, and 43.

It is further note that the dose of 4-hydroxy-2,2,6,6- tetramethylpiperidine-1-oxyl (TEMPOL = applicant's elected nitroxide species) of 0.1 to 300 mg/kg/day taught by Mitchell et al. for use as a protectant against oxidative stress in treating various conditions associated with oxidative stress such as reperfusion injury, myocardial infarction and strokes overlaps with the dose of TEMPOL exemplified in the instant (i.e. 1-300 mg/kg; see page 12, para. 0058).

In addition, it is the examiner's position that the sequence of first identifying a patient with ischemia, followed by administering TEMPOL, or alternatively, first administering TEMPOL, then identifying a patient with ischemia is within the skill of artisan skilled in the art (see claim 42).

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau, can be reached at 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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20 October 2008

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